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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/241,653	02/02/1999	HERMANN WAGNER	C1041/7002-H	8996

7590 01/02/2002

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EXAMINER	
ZARA, JANE J	
ART UNIT	**PAPER NUMBER**
1635	

DATE MAILED: 01/02/2002 24

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/241,653	WAGNER ET AL.	
	Examiner	Art Unit	
	Jane Zara	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____ .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 1-77 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 1-77 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C § 119(e) (to a provisional application)

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

This Office action is in response to the communications filed July 5, 2001 and on October 18, 2001, Paper Nos: 18, 21 and 23.

Claims 1-77 are pending in the instant application.

Request for Continued Examination

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on July 5, 2001 has been entered.

Withdrawn Rejections

Response to Arguments and Amendments

Rejection of claims 1-77 under 35 U.S.C. 112, first paragraph, is withdrawn in light of Applicants' amendments and arguments filed July 5, 2001 and October 18, 2001, Paper Nos. 19 and 23.

New Rejections

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

(e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371© of this title before the invention thereof by the applicant for patent.

Claims 1-12 and 14-77 are rejected under 35 U.S.C. 102(e) as being anticipated by Krieg et al.

Krieg et al (USPN 6,214,806) teach compositions and methods for inducing an antigen specific immune response comprising the administration of a CpG containing oligonucleotide of at least 8 nucleotides in length to a subject, which oligonucleotide optionally further comprises modified internucleotide linkages such as phosphorothioate linkages, which administration occurs either in combination with or prior to administration of an antigen, and which antigen comprises an allergen which is derived from an infectious agent, and which subjects include those that are leukopenic, neuropenic or immunocompromised, wherein the antigen specific response comprises a shift from a Th2 to a Th1 response in the organism following administration of the CpG containing oligonucleotide (See entire document, especially columns 3-6, 11, example 8 in columns 27-30; figures 8-14; claims 1, 8, 25, 31, 33, 34 and 37).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person

having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103© and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-77 rejected under 35 U.S.C. 103(a) as being unpatentable over Krieg et al (USPN 6,214,806) as applied to claims 1-12 and 14-77 above, and further in view of Krieg et al (USPN 6,207,646).

The claims are drawn to compositions and methods for inducing various phenotypes in a subject which are associated with a conversion from a Th2 to a Th1 mediated immune response, including induction of an antigen specific immune response and changes in leukocyte and lymphocyte populations and responses, comprising the administration of a CpG containing oligonucleotide of at least 8 nucleotides in length, and which oligonucleotide optionally further comprises modified internucleotide linkages such as phosphorothioate linkages, and which administration occurs prior to administration of an antigen, and which antigen is an allergen such as a polysaccharide or a nucleic acid molecule encoding an antigen, and which antigen is derived from an infectious agent.

Krieg et al (USPN 6,214,806) is relied upon as cited in the 102 rejection above.

The primary reference does not teach the administration of a nucleic acid molecule which encodes an antigen.

Krieg et al (USPN 6,207,646) teaches the induction of an antigen specific response in a subject comprising the administration of a CpG containing oligonucleotide and further comprising the administration of a nucleic acid encoding an antigen, wherein the antigen specific response comprises a shift from a Th2 to a Th1 response in the subject following administration of the CpG containing oligonucleotide (See especially claims 24 and 31-35).

The instant invention would have been obvious to one of ordinary skill in the art at the time the invention was made because Krieg et al taught methods and compositions for inducing an antigen specific immune response in an organism comprising the administration of a CpG containing oligonucleotide to a subject, either in combination with or prior to administration of an antigen to the subject, whereby a conversion from a Th2 to a Th1 immune response occurred in the subject, which immune response resulted in the display of various associated phenotypes in the subject, including the induction of an antigen specific immune response. Krieg et al have also taught such an induction from a Th2 to a Th1 response in a subject comprising the administration of a nucleic acid encoding an antigen in combination with administration of a CpG containing oligonucleotide. One of ordinary skill in the art would have been motivated to induce such an immune response from a Th2 to Th1 mediated immune response because, as taught previously by Krieg et al and others in the art, a Th1 mediated immune response results in

various in vivo effects in a subject, including decreased inflammation, decreased endotoxemia, and a general increase in the immune response in an organism, which increased immune response is measured in various ways, including changes in antibody forming capacity, stimulation of B cell, monocyte and killer cell responses, changes in the number of lymphocyte subpopulations, lymphocyte proliferation and in mixed leukocyte responses (See USPN 6,214,806 especially at columns 7-8) . One of ordinary skill in the art would have been motivated to administer a CpG containing oligonucleotide to an organism in order to induce a Th1 mediated immune response, either in combination with, before or after administration of an antigen because Krieg et al taught that the administration of CpG containing oligonucleotides induces an antigen specific immune response in an organism and decreases harmful side effects which would normally result from an organism's exposure to an antigen. One of ordinary skill in the art would have expected that such benefits which are imparted to an organism upon administration of a CpG containing oligonucleotide are achieved using various time frames between administration of the CpG containing oligonucleotide and administration of an antigen, including the simultaneous administration of the antigen and the oligonucleotide, as well as administration or exposure of the antigen to the organism after or before administration of the CpG containing oligonucleotide. One of ordinary skill in the art would also have expected that the administration of an antigen within these various time frames includes administration of nucleic acids encoding the antigen, which form of administration also provides the conversion of a Th2 to a Th1 mediated immune response, thereby providing the associated benefits described above. The effects provided by the

previously disclosed methods of treatment and which are specifically delineated in the claims of the instant application, are the result of the treatment methods previously disclosed by Krieg et al (comprising the administration of CpG containing oligonucleotides, in combination with, prior to, or after the administration of an antigen), and, absent evidence to the contrary, are effective independent of the source of immunosuppression or leukemic conditions of the subject, and are effective independent of the time frame which has lapsed between the administration of the CpG containing oligosaccharide and the administration of the antigen. One of ordinary skill in the art would have been motivated to provide the antigen in the form of a nucleic acid which encodes a protein antigen because, as disclosed previously by Krieg et al, the administration of a nucleic acid encoding an antigen provides for a prolonged half-life of the antigen in the organism, and also provides for an antigen specific immune response upon additional administration of a CpG containing oligonucleotide to the organism. One of ordinary skill in the art would have expected therefore that the administration of a nucleic acid encoding an antigen, in combination with or subsequent to the administration of a CpG containing oligonucleotide, induces a conversion from a Th2 to a Th1 mediated immune response in the organism, including the induction of an antigen specific immune response.

Therefore, the invention as a whole would have been prima facie obvious to one of ordinary skill at the time the invention was made.

Conclusion

Certain papers related to this application may be submitted to Art Unit 1635 by facsimile transmission. The faxing of such papers must conform with the notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 C.F.R. § 1.6(d)). The official fax telephone numbers for the Group are (703) 308-4242 and (703) 305-3014. NOTE: If Applicant *does* submit a paper by fax, the original signed copy should be retained by applicant or applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED so as to avoid the processing of duplicate papers in the Office.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to **Jane Zara** whose telephone number is **(703) 306-5820.** If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, John LeGuyader, can be reached on (703) 308-0447. Any inquiry regarding this application should be directed to the patent analyst, Katrina Turner, whose telephone number is (703) 305-3413. Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

ANDREW WANG
PRIMARY EXAMINER

JZ

December 28, 2001